Activation of γ-aminobutyric acidB receptors by baclofen improves visual temporal property of relay cells in the cat lateral geniculate nucleus

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Abstract

The role of γ-aminobutyric acidB (GABA B) receptors in spatial and temporal properties of the neurons was investigated in the cat dorsal lateral geniculate nucleus (dLGN) using flashing spot and drifting grating stimuli. Iontophoresis of baclofen, the selective GABA B receptor agonist significantly decreased the spontaneous and visual evoked responses (decreased to 38 ± 7%), in which only the sustained component was suppressed sharply. Baclofen affected neither the center-surround antagonism of receptive fields nor the optimal spatial frequency of stimulating gratings. However, baclofen shortened cells’ response duration and elevated their temporal frequencies that evoked the maximum and the half maximum response. In contrast, 2-OH-sacrofen, a GABA B antagonist showed no significant effect on dLGN cells’ spatio-temporal properties. In conclusion, the activation of GABA B receptors may improve the temporal response properties of dLGN cells’ via the sustained pathway, rather than change the spatial properties.

Keywords: Baclofen; γ-aminobutyric acidB receptor; Lateral geniculate nucleus; Receptive field; Temporal property; Cat

Inhibition is crucial for cells in the dorsal lateral geniculate nucleus (dLGN) in controlling the relay of visual information from the retina to the cortex and participating in the thalamo-cortical oscillations [5,18]. Three types of γ-aminobutyric acid (GABA)-ergic receptor mediated inhibitory post-synaptic potential (IPSP) have been described previously. The early C1-dependent IPSPs are mediated by GABA A or GABA C receptors, of which the former plays a key role in sharpening the response properties of geniculate cells such as center-surround antagonism [17] and orientation tuning [19]. The GABA B receptors mediated late IPSPs are relatively slow and differ fundamentally from that of GABA A receptors. GABA B receptors are located in pre- and/or post-synaptic membranes, and coupled respectively to various Ca 2+ and K + channels presumably through both a membrane-delimited pathway and a pathway involving second messengers [4,13].

In the primary visual cortex, the GABA B receptor mediated inhibition enhances the orientation selectivity of the sustained response [1]. The GABA B receptors have been shown in thalamus, particularly in the dLGN. There is a higher density of GABA B binding sites in dLGN than in the ventral LGN [3]. GABA B receptors also participate in the oscillation of dLGN [5,18]. However, in the visual information processing, the role of GABA B receptors in the spatio-temporal properties of dLGN neurons in vivo is still unclear. The purpose of this study is to elucidate this issue using electrophysiological technique combined with local administration of baclofen (p-chlorophenyl GABA), a selective GABA B agonist.

Seven adult cats were prepared for single unit recording as described previously [16]. Animals were kept slightly anesthetized and paralyzed throughout the experiments. A computer driven Picasso image synthesizer (Innisfree,
Fig. 1A shows the PSTHs of a typical cell’s responses to flashing spots of increasing diameter before and during baclofen administration. During baclofen injection, the sustained component almost disappeared compared with the control, while the transient component of the visual responses changed little. The most prominent inhibitory effect appeared at about 120 ms and later after the onset of visual stimulus in eight neurons measured, corresponding to the size of the cell’s receptive field center, and then decayed with increasing diameter due to the surround inhibition. It is noteworthy that both the peak and the count response curves were similar in shape. Although the count response was reduced 2.5-fold by baclofen (open square curves, upper in Fig. 1B), either the diameter of the flashing spot that evoked the maximum response or the time course of the response decreased with increased diameter kept unchanged during baclofen application. This suggests that the center-surround antagonist mechanism of the receptive field is unaffected by the baclofen activation of GABA_B receptors.

To study whether GABA_B receptors contribute to the spatial property of the relay cells, we measured the spatial frequency tuning curves before and during baclofen injection using drifting sinusoidal grating stimuli (Fig. 2). Obviously, baclofen injection reduced the cell’s response, but had little effect on the shape of the high part of the spatial frequency-tuning curve. Since a cell’s spatial resolution of gratings is closely related to the center mechanism of its receptive field, thus, this is quite in agreement with the above finding that baclofen did not affect the spatial center-surround structure of receptive fields.

Baclofen made the time course of PSTHs narrower, while the peak response changed little, as shown in Fig. 3A. Inter-
Interestingly, the optimal temporal frequency in temporal frequency tuning curves shifted to the right (higher frequency direction) during activation of GABA\textsubscript{B} receptors by baclofen presumably due to the shortening of response time course (Fig. 3B). The improvement in temporal frequency property caused by baclofen was prominent (\textit{t}-test, \( P < 0.05 \)) in all seven neurons tested. The histograms in Fig. 3C summarize the effects of baclofen on temporal frequency in these cells. Baclofen significantly increased the optimal temporal frequencies that evoked the maximum responses and the higher frequency that evoked the half maximum response.

We also administrated the GABA\textsubscript{B} receptor antagonist 2-OH-saclofen in the dLGN, however, neither the spontaneous nor the visual evoked responses changed significantly during drug application in dLGN. There are some studies suggesting that 2-OH-saclofen exhibits partially agonist properties in rat dLGN, as suggested by Emri [6] though 2-OH-saclofen had electrophysiological effect in many brain areas such as visual cortex [1] and superior colliculus [2] in vivo.

In this study we demonstrated the first evidence that activation of GABA\textsubscript{B} receptors by baclofen improved the temporal properties of relay cells of dLGN in the cat without influence to the cells’ spatial discrimination, although the sustained response component was reduced. This suggests that the GABA\textsubscript{B} receptor-mediated inhibition may play an important role in temporal property within the cat dLGN.

The results showed that GABA\textsubscript{B} receptor mediated inhibition was limited to the long latency (>120 ms) sustained response. It is consistent with the notion that the GABA\textsubscript{B} receptor operates via a ‘slow’ G-protein coupled second messenger system [4]. Perceptual and single unit studies have revealed the existence of sustained and transient channels in visual system (for review, see Ref. [12]). Compared with the previous report that bicuculline affected primarily the transient responses of dLGN neurons [7,14] our results suggest that the inhibitions mediated by GABA\textsubscript{A} and GABA\textsubscript{B} receptors may modulate signals through the transient and sustained pathways, respectively.

Previous work suggested that GABA\textsubscript{A} receptors played
densities of GABA B receptors on the different neurons. The difference implies that the transient components may carry more spatial information than the sustained one. Our finding that baclofen injection elevated the optimal temporal frequency of cells’ responses indicates a kind of nonlinear interaction within the dLGN, and is in agreement with the observation in the visual cortex by Pfleger and Bonds [15].

GABA_B receptors were located either in pre-synaptic or in post-synaptic membranes in many brain areas [3,6,9,11]. Our study could not distinguish whether the effect of baclofen is pre- and/or post-synaptic in the dLGN, however, some evidence suggested that postsynaptic GABA_B receptors were not activated by endogenous GABA in visual pathway [6]. Our observation showed that there were six neurons silenced by baclofen, while the majority of cells still kept some degree of response even when a large injection current was used. The difference implies that the densities of GABA_B receptors on the different neurons may vary significantly. On the other hand, the subtypes of baclofen-insensitive GABA_B receptor [8] may also exist in the relay cells in cat dLGN, as Yamada suggested in other brain areas [20].

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